REMARKS

In the Office Action mailed March 21, 2002, the claims were subject to a restriction requirement. Claims 39-60 were rejected under 35 U.S.C. 112, first paragraph. Claims 40-51 were rejected under 35 U.S.C. 112, first paragraph. Claims 39, 60 and 61 were rejected under 35 U.S.C. 112, second paragraph. Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b). Claims 39-59 were rejected under 35 U.S.C. 103(a) as being allegedly obvious over Spencer. Claims 39-59 were rejected under 35 U.S.C. 103(a) as allegedly obvious over Petering. Claims 62 and 63 were said to contain allowable subject matter.

The Amendments

This response rewrites claims 62 and 63 as independent. This response cancels claim 61 without prejudice. Claim 39 has been amended to add the limitation that the composition includes a component selected from the group consisting of biologically active protein, blood, and blood constituents. This amendment is supported by the specification as filed, including page 6, lines 17-20; and page 8, line 13 through page 9, line 2, and claim 1. Claim 39 has also been amended on page 53, line 9 to clarify the groups that are optionally substituted by expressly writing the groups in the claim. Claim 39 has been amended on page 55 to clarify the limitation that R2 does not contain a carbonyl group. This amendment is intended to more clearly describe the limitation. Claim 39 has been amended on page 55 to include the limitation that R1 and R2 are not both methyl groups when R3, R4, R5 and R6 are H. This limitation is supported by the specification as filed, including page 11, lines 12-14. Claim 39 has been amended on page 57 to clarify the limitation when R2 is not octadecyl or undecyl. This amendment is supported by the specification as filed, including page 11, lines 12-14. All amendments to the claims are supported by the original claims and specification as filed. No new matter is added.

Restriction Requirement

In response to the Restriction Requirement, which restricted the claims to Group I, claims 1-38, drawn to methods of using compounds, and Group II, claims 39-63, drawn to compounds, Applicants confirm the election made by telephone on March 4, 2002, of Group II, claims 39-63, with traverse. The Office Action stated that the claims are related as product and process of use. Since the same compounds are used in both Groups, it is believed a search of the two groups would not be burdensome. Reconsideration and withdrawal of the restriction requirement is therefore respectfully requested.

Rejection of claims 39-60 under 35 U.S.C. 112, first paragraph

Claims 39-60 were rejected under 35 U.S.C. 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The Office Action states "the claims are not commensurate in scope as to the possibilities for the substituent 'straight chain or cyclic sacharides,' 'amino acid groups,' 'alkylating Agents,' 'substitutents that cause the compound to be substantially nonreactive to microorganisms' in the various R definitions. They are open-ended and all encompassing. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these broad claims, which embrace a diversity of substituents at various locations on the isoalloxazine ring."

Applicants can not find any reference to "substituents that cause the compound to be substantially nonreactive to microorganisms" in claims 39-60. It is believed this portion of the rejection is directed to claim 61. In response to this portion of the rejection, claim 61 has been cancelled.

It is noted the terms "straight chain or cyclic saccharides", "amino acid groups", "alkylating agents" have art-recognized meanings. The term "straight chain or cyclic saccharides" is well defined in the art. The term is defined in the specification on page 20, line 20 through page 21, line 2 to include "mono-, di- and poly-, straight chain and cyclic saccharides

that are optionally substituted with an amino group which is optionally acetylated." In addition, the definition of "straight chain or cyclic saccharides" is found in general biochemistry textbooks, for example the pages shown in Exhibit A from Voet and Voet, Biochemistry, 1990, John Wiley & Sons, New York, pages 245-260 and Exhibit B, pages 214-215 of Daintith, ed., The Facts on File Dictionary of Chemistry, 1988, Charles Letts & Co., Ltd.

The term "amino acid group" is well defined in the art as "derivatives of carboxylic acids in which a hydrogen atom in an aliphatic acid has been replaced by an amino group" (Daintith, ed., The Facts on File Dictionary of Chemistry, 1988, Charles Letts & Co., Ltd, page 13, attached as Exhibit C).

The term "alkylating agent" is defined in the specification on page 23, lines 24-25 as "a compound that reacts with amino acid residues and nucleic bases and inhibits replication of microorganisms." The term "alkylating agent" is well known in the art as a functional term. The attached Exhibits D and E show that the mechanism of action of alkylating agents is well defined, and those of ordinary skill in the art would recognize the presence of an alkylating agent.

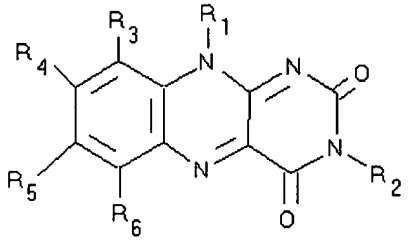
In view of the above, anyone of ordinary skill in the art would be able to determine if a particular compound contained a "straight chain or cyclic saccharide", an "amino acid group" or an "alkylating agent."

The Office Action then states there is insufficient guidance in the specification to enable a person skilled in the art to make and use the invention commensurate in scope with the claims. The Office Action states only compounds wherein R1 and R5 are methyl, R2, R3, and R6 is H, R4 is C(O)OR, $N(CH)_2W(CH)_2Cl$ have been made.

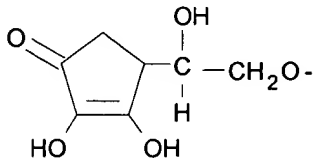
The molecules claimed in claims 39-60 can be easily prepared by one skilled in the art without undue experimentation using art-known methods. The inventiveness of these compounds lies in identifying structures which work for purposes of neutralizing biological

contaminants, not in any special methods for making the compounds.

Specifically, the following discussion shows how compounds claimed herein are synthesized using methods known to the art. Methods are known in the art for preparing compounds having the structure:

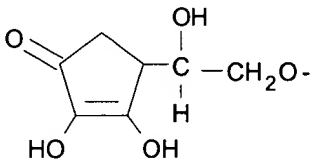


wherein R1, R2, R3, R4, R5 and R6 are, independently from one another, selected from the group consisting of hydrogen, -OH, -NH2, -SO4, -PO4, -Cl, -Br, -I, straight chain or cyclic saccharides with 5 or 6 carbon atoms;



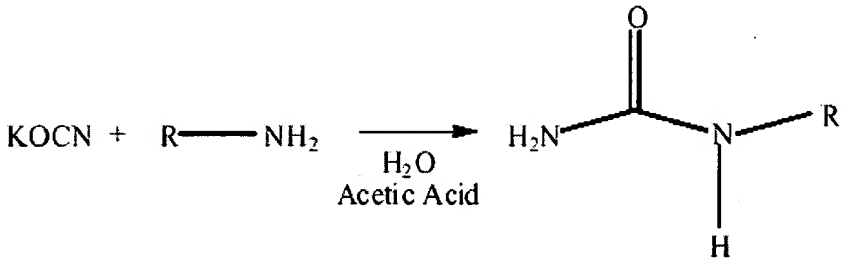
amino acid groups; optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms said groups optionally substituted with one or more of -O-, -S-, -OH, $-NH_2$, $-SO_4$, $-PO_4$, -Cl, -Br, -I;

$-NR^a-(CR^bR^c)_n-X$ wherein X is a halogen selected from the group consisting of chlorine, bromine and iodine, R^a, R^b and R^c are, independently of each other, selected from the group consisting of hydrogen; straight chain or cyclic saccharides with 5 or 6 carbon atoms;

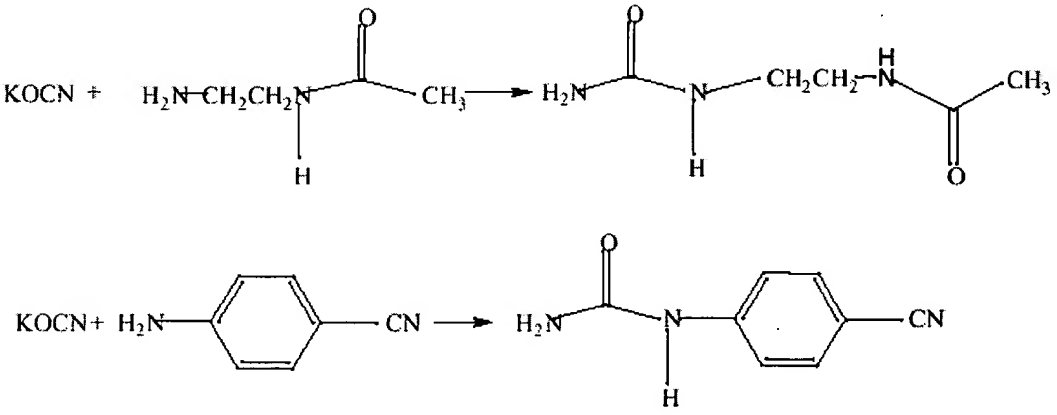


amino acid groups; optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms optionally substituted with one or more of -O-, -S-, -OH, $-NH_2$, $-SO_4$, $-PO_4$, -Cl, -Br, -I; and halogen selected from the group consisting of chlorine, bromine and iodine; and salts of the foregoing wherein n is an integer from 0 to 20.

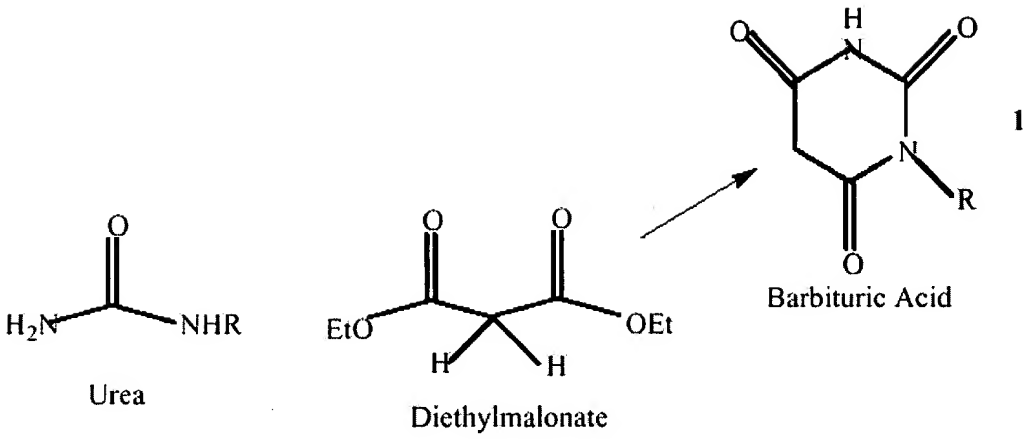
Ureas are synthesized, in general, using KOCN and amine. Balsamini, C.; Bedeni, A.; Diamantini, G.; Spadoni, G.; Tarzia, G.; Tontyni, A.; DiFabio, R.; Donati. *Il Farmaco*. 1999, 54, 101.



The R group can be alkyl or aryl. The R substituent can contain an alkyl or aryl sub-group containing a water-soluble group or a masked water soluble group such as cyano or acetamide as shown below. The cyano group is reduced to a CH_2NH_2 group by reduction with hydrogen over a catalyst after the alloxan-ortho-phenylene diamine condensation reaction (*vide infra*). Similarly the acetamido group is hydrolyzed with acid or base catalyst to release an amino group after the condensation reaction has been performed.



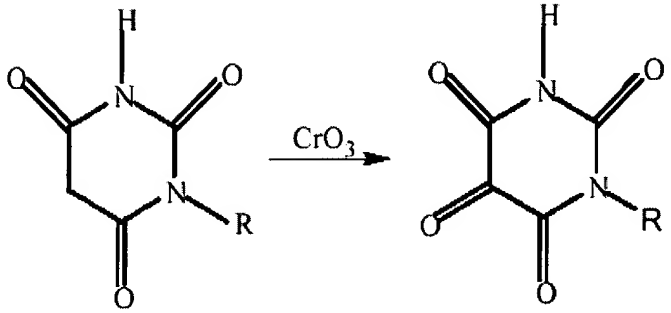
Ureas are condensed with diethylmalonate to form barbituric acid derivatives **(1)**.



1

O.J.B. Dickey and A.R. Gro, Org. Syn. Coll Vol II, 60, 1999

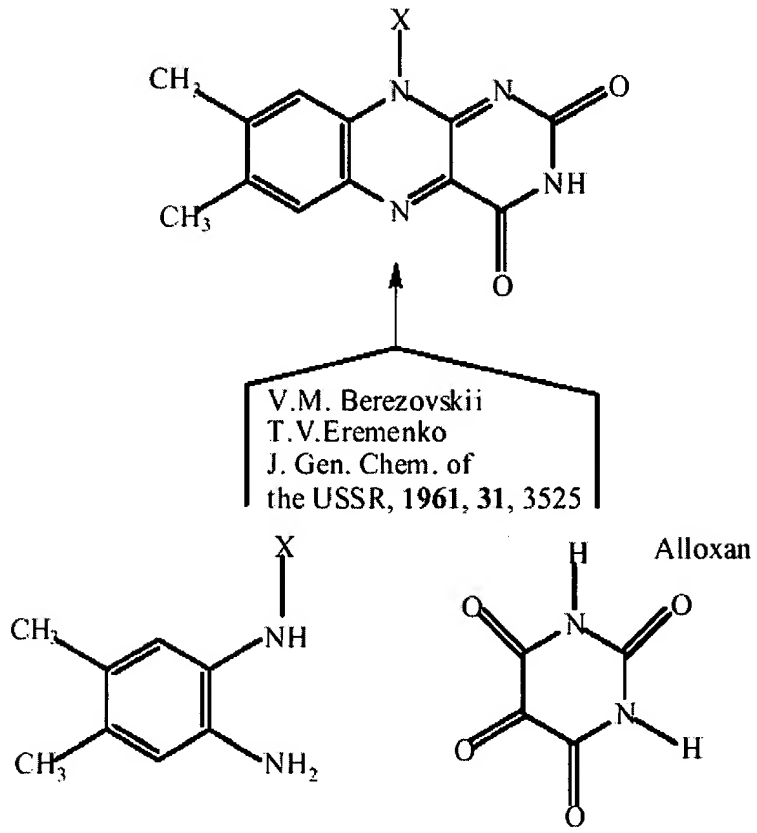
The barbituric acid derivatives are oxidized to form derivatives **(2)** of alloxan.



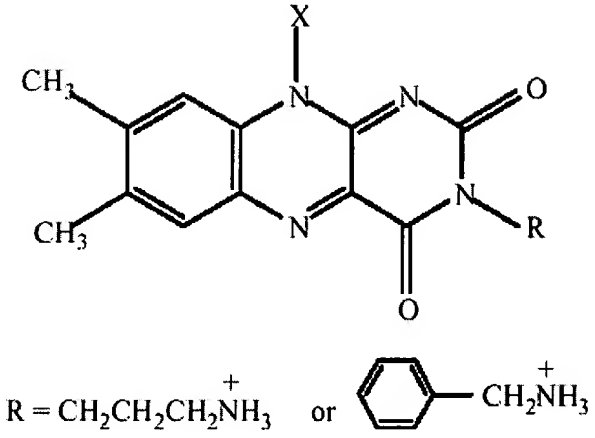
2

A.V. Holmgren and W. Wenner, Org. Syn. Coll Vol IV 23 (1963).

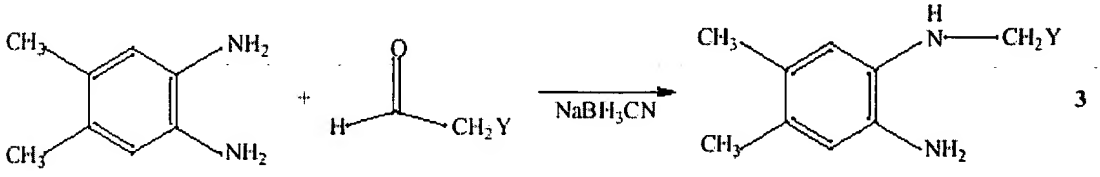
Alloxan and ortho-phenylene diamines condense to form isoalloxazines.



In this synthesis X can be ribityl to form riboflavin, or X = methyl to form lumiflavin.



When a substituted alloxan such as **2** is used, then a riboflavin derivative with substitution R (i.e. R2 above) at the nitrogen of the right hand ring (N_3) is formed ($R \neq H$). The water soluble side chain is then released by removal of the masking group.
Ortho-phenylene diamines **3** is functionalized easily by reductive amination following literature procedures.

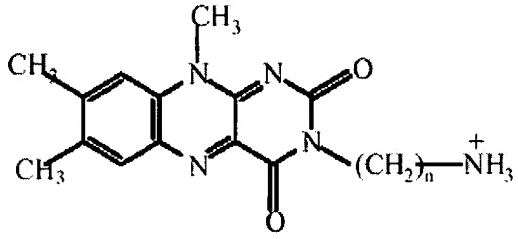


3

Thus, a library of structures with various alkyl or aryl groups X (as defined by R1 above) is prepared by condensing alloxanes **2** with **3**. Similarly, phenyl diamines having various substituents as set forth above at the R3-R6 positions may be used to form isoalloxazine derivatives having the structures discussed above.

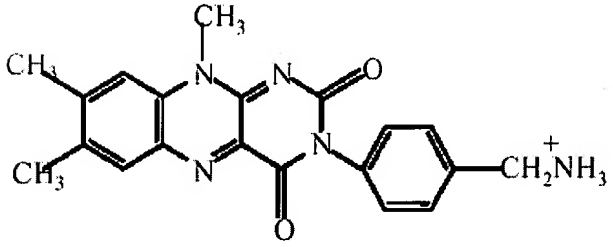
The following lead structures **4-6** are efficacious because they have a permanent positive charge and thus, superior binding to DNA relative to electrically neutral flavins such as riboflavin which bind nucleic acids poorly.

4



n=2-4

5



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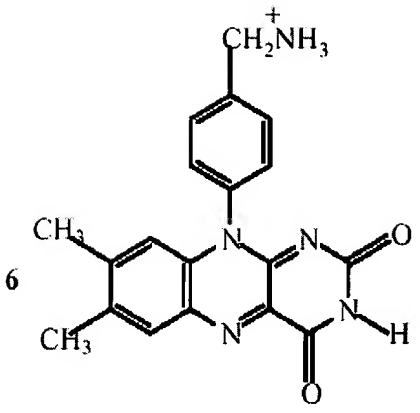


These compounds can be mixed with suitable pharmaceutical carriers.

The Office Action then states that no testing results are provided for any of the compounds listed in the specification. Since photoirradiation methods are known in the art, e.g., as described in publications cited in the Background Section at page 2, first and second full paragraphs, one skilled in the art can easily, and without undue experimentation, substitute the compositions claimed herein for those of the prior art in the methods described in the prior art. As shown in the attached "Mechanisms of Action of Isoalloxazine Derivatives for Biological Decontamination," (Exhibit F) the usefulness of the claimed compositions is well-supported by scientific reasoning.

It is not considered necessary to separately show each possible compound covered by the claims as this would be extremely burdensome. In view of the above scientific evidence, there is more than adequate teachings of how to make and use the claimed invention. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 40-51 under 35 U.S.C. 112, first paragraph

Claims 40-51 were rejected under 35 U.S.C. 112, first paragraph as allegedly not providing enablement for a plurality of R1, R2, R3, R4, R5 and R6 being neither methyl not H.

Applicants respectfully traverse this rejection. It is well known to one of ordinary skill in the art how to make isoalloxazine derivatives with more than one non-methyl or non-hydrogen substituent. The references cited by the Office Action and the discussion above show this fact to be true. For example, the isoalloxazine compounds described in United States Patent 3,920,650 (Spencer) disclose methods of making compounds with more than one non-methyl or non-hydrogen substituent. In addition, the isoalloxazines described in United States Patent 2,825,729 (Petering et al.) describe isoalloxazine derivatives with more than one non-methyl or non-hydrogen substituent.

In view of the above, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 39, 60 and 61 under 35 U.S.C. 112, second paragraph

Claims 39, 60 and 61 were rejected under 35 U.S.C. 112, second paragraph, as being allegedly indefinite.

Claim 60 was said to be vague and indefinite in the metes and bounds of the term "alkylating agents." The term "alkylating agents" is well-known in the art, as shown above.

The last three lines of claim 39 on page 53 was said to be unclear. The last three lines of claim 39 on page 53 are intended to specify the optional substituents for the alkyl, alkenyl, alkynyl or aryl groups. Claim 39 has been clarified to specifically list the groups which are optionally substituted. This amendment is believed to overcome this portion of the rejection.

Claim 61 was said to be vague and indefinite regarding the substituents for R1-R6. Claim

61 has been cancelled, so this rejection is moot.

In view of the above amendments and arguments, it is believed the rejection of claims 39, 60 and 61 were rejected under 35 U.S.C. 112, second paragraph is overcome. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims 39, 49-53 and 58 under 35 U.S.C. 102(b)

In the Office Action, claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by several references. Claims 49-53 and 58 are dependent on claim 39, so this response will be directed to claim 39, but will apply to claims 49-53 and 58.

Claim 39 has been amended to add the limitation that the composition includes a blood product, as well as the blood product additive described by the structures in claim 39. No reference cited includes a blood product, so all rejections under 35 U.S.C. 102(b) are moot. However, the compounds claimed in claim 39 are not anticipated by the references cited, as discussed below.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Tyrakowska et al. (J. Photochem. Photobiol., 1993). The Office Action states "Tyrakowska teaches the compound of the instant invention where instant R is (CH2)10-H (see Scheme 1)." Using the variables in the present invention, Scheme 1 of Tyrakowska shows an isoalloxazine where R1 is H; R2 is an undecyl group; R4 and R5 are methyl; and R3 and R6 are hydrogen. This compound does not anticipate claim 39. In claim 39 on page 54, line 9, the limitation that R1 can not be H is found. Also, on page 57, lines 5-6, the limitation that "R2 is not octadecyl or undecyl when R4 and R5 are methyl and R1, R3 and R6 are hydrogen" is found. Therefore, the compounds of Tyrakowska are not claimed in the present invention.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Koziol et al. (Inst. Commod. Sci., 1991). The Office Action states "Koziol teaches the

compound of the instant invention where instant R is methyl and ribityl; R1 is H, Me, undecyl, octadecyl." The compounds disclosed in Koziol are 10-methyl-isoalloxazine; 3,10-dimethylisoalloxazine; 3,7,8,10-tetramethylisoalloxazine; riboflavin; 3-undecyl-7,8,10-trimethylisoalloxazine; and 3-octadecyl-7,8,10-trimethylisoalloxazine. 10-methyl-isoalloxazine is not included in the claims of the present invention (page 55, line 25 to page 56, line1). 3,10-dimethylisoalloxazine is not included in the claims of the present invention (newly added limitation to claim 39). 3,7,8,10-tetramethylisoalloxazine is not included in the claims of the present invention (page 55, lines 21-22). Riboflavin is not included in the claims of the present invention (page 54, lines 9, 10). 3-undecyl-7,8,10-trimethylisoalloxazine and 3-octadecyl-7,8,10-trimethylisoalloxazine are not included in the present invention page 57, lines 5-6).

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Schoo et al. (Macromolecules, 1992). The Office Action states "Schoo teaches the compound of the instant invention (see Figure 5 on P. 1635)." Figure 5 of Schoo teaches the compound where R2 contains a benzyl group when R1, R4, and R5 are methyl, and R3 and R6 are hydrogen. This compound is not included in claim 39 (see page 57, lines 6-7 "provided that R2 is not a benzyl group when R1, R4 and R5 are methyl; and R3 and R6 are hydrogen." As known in the art, a benzyl group is: -CH2-phenyl.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Herfeld et al. (Anti-Cancer Drug Des., 1998). The Office Action states the compounds of the subject invention read on the compounds shown on the CAPLUS search report and RN 144446-13-9 and 144446-14-0. These compounds are not included in claim 39 (see page 57, lines 7-8 "provided that R1 or R2 do not contain a poly(pyrrolecarboxamide) group").

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Herfeld et al. (Lab. Chim. Ther., Fac. Sci. Pharm. Biol., 1994). The Office Action states the compounds of the subject invention read on the compounds shown on the CAPLUS search report. These compounds are not included in claim 39 (see page 57, lines 7-8 "provided that R1

or R2 do not contain a poly(pyrrolecarboxamide) group").

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Grimmer et al. (US 5,095,115). The Office Action states "Grimmer teaches the compound of the instant invention wherein R1 is a phosphate group optionally substituted by a chlorine." The compounds of Grimmer are not included in claim 39. First, the compounds shown in Grimmer contain straight chain alkyl groups where the second carbon of the chain is substituted with -OH as R1. It is noted that alkyl groups may be optionally substituted with -PO4 groups, which is shown in Grimmer. These compounds are excluded from claim 39 on page 54, lines 9-10. Also, page 57, lines 16-18 excludes compounds where R1 is a two to six member alkyl chain terminated with a sulfate radical, a phosphate radical or an acyloxy radical. These exclusions exclude the compounds of Grimmer.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Spencer et al. (US 3,920,650). The Office Action states "Spencer teaches the compound of the instant invention wherein R3 is hydroxyethyl or R10 is phenyl (see table on Col. 7 and 8)." Translating the compounds of Spencer into the variable use of the present invention, the compounds of Spencer are those where R1 is ethyl, propyl, isopropyl, butyl, pentyl, hexyl, phenyl, benzyl, phenethyl, napthyl, p-tolyl, p-ethylphenyl, p-anisyl, p-ethoxyphenyl, p-butoxyphenyl, 3,4-dichlorophenyl, methoxyethyl or ethoxyethyl, R2 is hydrogen, methyl, hydroxyethyl or benzyl, and R5 is bromo, chloro, nitro or trifluoromethyl. These compounds are excluded from claim 39 on page 57, lines 8-12.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Yagi et al. (US 3,189,598). The Office Action states Yagi teaches the compund of the instant invention (see Col. 1). Yagi teaches the compound where R1 is a five carbon alkyl chain where four carbons are substituted with -O-COR where RCO is a straight chain alkanoyl group containing from 4 to 20 carbon atoms. These compounds are excluded from claim 39 on page 57, lines 12-14.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Kuhn et al. (US 2,111,491). The Office Action states Kuhn teaches the compund of the instant invention wherein R1 is a phosphate group. The compounds disclosed in Kuhn are excluded from claim 39 on page 57, lines 14-16.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Petering et al. (US 2,825,729). The Office Action states Petering teaches the compound of the instant invention in Examples 1-42. Petering discloses compounds wherein R1 is a 2 to 6 member alkyl chain terminated with an acyloxy radical, the acyl group of which is derived from an organic acid with not more than eighteen carbon atoms, a sulfate radical or a phosphate radical. The compounds disclosed in Petering are excluded from claim 39 on page 57, lines 16-18.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Funk et al. (US 2,654,735). The Office Action states Funk teaches the compound of the instant invention wherein R1 contains a phosphate group (see Example 1 on col. 4). The compounds disclosed in Funk have -OH substituted on the second carbon of a straight chain alkyl group as R1. These compounds are excluded from claim 39 on page 54, lines 9-10.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Dickinson et al. 132: 10368. Dickinson et al. discloses a compound where R1, R4 and R5 are methyl, and R2 is acetyl. The group "acetyl" is -C(O)Me and is also known as carboxymethyl. The compound disclosed in Dickinson is excluded from claim 39 on page 55, lines 22-23.

Claims 39, 49-53 and 58 were rejected under 35 U.S.C. 102(b) as being anticipated by Herfeld et al. (Bioconjugate Chem., 1994). The compounds on the CAPLUS search report having RN 14446-18-4-9 and 144446-17-3 disclose groups where R2 contains a carbonyl group. The exclusion in claim 39 on page 53, lines 22-23 "R2 is not carboxymethyl when R1, R4 and R5 are methyl and R3 and R6 are hydrogen" has been clarified to specify that R2 does not

contain a carbonyl group. This amendment is supported by the specification and claims as filed, including the limitation in claim 39 originally appearing, and the specification on page 14, line 10.

In view of the above, the references cited do not anticipate claim 39. The other rejected claims, claims 49-53 and 58 are dependent on claim 39 and include all limitations therein. Reconsideration and withdrawal of the rejections is respectfully requested.

Rejection of claims 39-59 under 35 U.S.C. 103(a)

Claims 39-59 were rejected under 35 U.S.C. 103(a) as being allegedly obvious over Spencer. The Office Action stated:

> Spencer et al. teach a generic group of isoalloxazine derivatives (See formula I, Col. 1). . . In addition to Compounds I-XXVI which anticipate the claims as discussed in the above 102 rejection the reference compounds differ only in the nature of substituent for R3, R7, R8, and R10. However, the compounds of the instant invention are generically embraced by Spencer in view of the equivalence of hydrogen, phenyl bromo, propyl, etc.

Applicants respectfully disagree. As discussed above, the claims of the subject invention are not anticipated by Spencer. The non-toxic composition disclosed in claim 39 includes a) a blood product and b) a blood product additive photosensitizer. This composition is not disclosed in the Spencer reference, nor suggested by the reference. The Spencer reference teaches certain isoalloxazines which are useful as antibacterial agents for use as "dusts, solutions, suspensions, sprays, unguents and the like" (column 1, lines 43-45). The Spencer reference does not disclose or suggest any inclusion of a blood product. There is no disclosure in Spencer about using the isoalloxazine derivatives disclosed in Spencer for use as a blood additive, and no discussion or disclosure in Spencer about administering the isoalloxazine derivatives disclosed in Spencer to a patient. Also, there is no disclosure in Spencer regarding the toxicity of the compounds. The compositions of matter disclosed by Spencer would not be suitable for human internal pharmaceutical use, as lacking the purity required. In addition, there is no disclosure in Spencer

regarding the use of light for inactivation of bacteria. These are critical differences between the disclosure of Spencer and the present invention.

There is no evidence presented for the Examiner's statement that hydrogen, phenyl bromo, propyl, etc are equivalent. According to the MPEP, section 2144,09, structurally similar groups include position isomers or homologs (compounds differing regularly by the successive addition of the same chemical group). Hydrogen, phenyl bromo and propyl are neither position isomers nor homologs, and have very different chemical structures. For example, phenyl bromo and hydrogen are markedly different, since phenyl bromo is a relatively large aromatic structure with a halogen and hydrogen is small and has no halogen or aromatic structure.

In order for a *prima facie* case of obviousness to be made, there must be a suggestion or motivation in the reference itself to modify the reference, there must be a reasonable expectation of success and the prior art reference must teach or suggest all claim limitations (MPEP 2142). In this case, there is no suggestion or motivation in Spencer to modify the reference to include a blood product, and no suggestion or motivation in Spencer to use any substituent other than those specifically listed in Compounds I-XXVI.

The Office Action states that "one of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. See *In re Susi*." This statement is incorrect, since the claimed compositions can not be selected from the compounds in the reference as the compounds in the reference do not include a blood product. There is no expectation of success in making any changes to the structures in Spencer because there is no guidance in making any compounds other than those disclosed in Spencer. The Spencer reference does not teach or suggest all claim limitations, as discussed above. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 39-59 were rejected under 35 U.S.C. 103(a) as allegedly obvious over Petering. The Office Action stated:

> Petering et al. teach a generic group of isoalloxazine derivatives (See formula I, Col. 1), in particular, where instant R1 is member selected from the (a), (b), and (c) substituents. In addition to Compounds which anticipate the claims as discussed in the above 102 rejection, the reference compounds differ only in the nature of substituent for R1, R2, R3, and R5. However, the compounds of the instant invention are generically embraced by Spencer in view of the equivalence of acyloxy, sulfate, phosphate radicals, etc. Thus, one of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.

Petering discloses [ω-hydroxyalkyl]-isoalloxazine esters of phosphoric, sulfuric or an organic acid containing not more than eighteen carbon atoms used for antimetabolite activity, for example riboflavin antagonists (col. 1, lines 61-64). Petering also discloses the compounds have anti-psittacosis activity (col. 1, lines 64-65). As discussed above, the compounds of Petering do not anticipate the compositions of the subject invention.

No evidence has been presented for the statement in the Office Action that acyloxy, sulfate, phosphate radicals, etc. are equivalent. Each substituent listed has a very different structure. Applicants respectfully request clarification of what is intended by the phrase "etc." and request evidence of the equivalence of the structures.

There is no disclosure or suggestion in Petering of the use of a blood product as a component in a composition. There is no suggestion or motivation in the disclosure of Petering to use the compounds disclosed as blood additive photosensitizers for inactivating microorganisms, and Petering does not teach or suggest the limitation in the claims that the compound is a blood additive for inactivating microorganisms. The reference, in fact, teaches against the use of the disclosed compounds as blood additive photosensitizers, an activity shared with riboflavin, since it teaches that the compounds are riboflavin antagonists. Therefore, no

prima facie case of obviousness has been made.

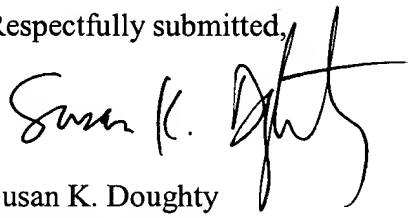
There is no suggestion in either of the references cited to modify the references to include a blood product in addition to an isoalloxazine compound. The invention as claimed in the present invention would not have been obvious to one of ordinary skill in the art. Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above arguments and evidence, it is believed that all objections and rejections of the claims have been overcome, and claims 39-63 are believed to be allowable. Reconsideration and withdrawal of the rejections and objections is respectfully requested. If there are any issues remaining, the Examiner is respectfully requested to telephone the undersigned.

This amendment is accompanied by a Petition for Extension of Time (two months) and a check in the amount of $400.00 as required under 37 C.F.R. 1.17(a)(2) for a large entity. If the amount submitted is incorrect, however, please charge any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,



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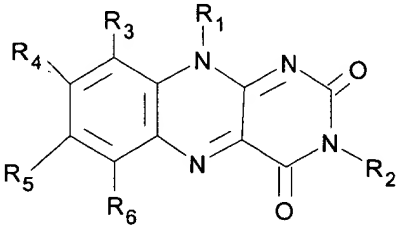
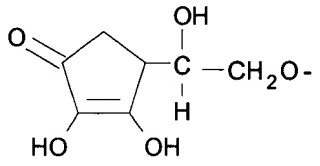
lla:62

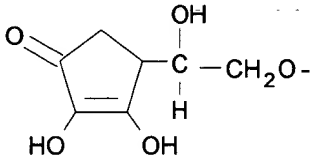
39. (once amended) A non-toxic composition comprising: (a) a component selected from the group consisting of biologically active protein, blood, and blood constituents; and (b) a blood product additive photosensitizer for inactivating microorganisms suitable for administration to a patient having the structure:



wherein R1, R2, R3, R4, R5 and R6 are, independently from one another, selected from the group consisting of hydrogen; -OH; -NH_2; -SO_4; -PO_4; -Cl; -Br; -I; straight chain or cyclic saccharides with 5 or 6 carbon atoms;

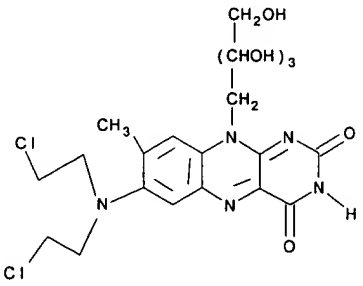


amino acid groups; optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms said alkyl, alkenyl, alkynyl or aryl groups optionally substituted with one or more of -O-, -S-, -OH, -NH_2 , -SO_4 , -PO_4, -Cl, -Br, -I; -NR^a-$(CR^bR^c)_n$-X wherein X is a halogen selected from the group consisting of chlorine, bromine and iodine, R^a, R^b and R^c are, independently of each other, selected from the group consisting of hydrogen; straight chain or cyclic saccharides with 5 or 6 carbon atoms;

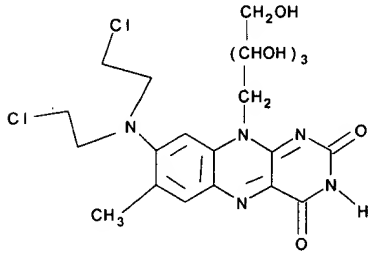


amino acid groups; optionally substituted alkyl, alkenyl, alkynyl or aryl groups with from 1 to 20 carbon atoms said groups optionally substituted with one or more of -O-, -S-, -OH, $-NH_2$, $-SO_4$, $-PO_4$, -Cl, -Br, -I; and halogen selected from the group consisting of chlorine, bromine and iodine; and salts of the foregoing wherein n is an integer from 0 to 20;

provided that R1 is neither H nor -OH nor a straight chain alkyl group where the second carbon of the chain is substituted with -OH or =O except that the compound may be

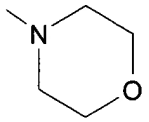


or



and provided that R1, R4, R5 are not all methyl groups when R2, R3 and R6 are hydrogen and R1 is not a 2-, 3-, 4- or 5- carbon straight chain alkyl that terminates in -OH, -COH, or -H when R2, R3 and R6 are H, and R4 and R5 are CH_3; provided that R1 is not -OH or a straight chain alkyl group where the second carbon of the chain is substituted with -OH or =O; and R1 is not a 2-, 3-, 4- or 5-

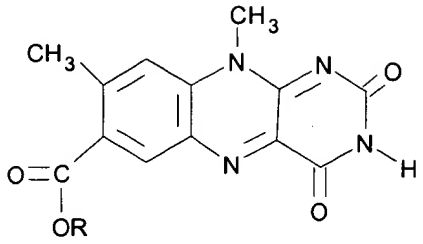
where the second carbon of the chain is substituted with -OH or =O; and R1 is not a 2-, 3-, 4- or 5-carbon straight chain alkyl that terminates in -OH, -COH, or -H when R2, R3 and R6 are H, and R4 and R5 are CH_3; R1 is not - CH_2CH_2-$(CHOH)_2$-CH_3 or -CH_2CH_2-$(CHOH)_2$ -CH_2SO_4 or 1'-D-sorbityl or 1'-D-dulcityl or 1'-D-rhamnityl or 1'-D,L-glyceryl or -CH_2-O-C(O)-CH_3 or -CH_2-O-C(O)-CH_2CH_3 or 2', 3', 4', 5'-di-O-isopropyridene-riboflavin or 8-aminooctyl when R2, R3 and R6 are H and R4 and R5 are CH_3; R1 is not 1'-D-sorbityl or 1'-D-dulcityl when R4 and R5 are both chlorines and when R2, R3 and R6 are all hydrogens; R5 is not ethyl or chloro when R1 and R4 are methyl and R2, R3 and R6 are all hydrogens; R4 and R5 are not both methoxy or both tetramethylene when R1 is methyl and R2, R3 and R6 are all hydrogens; R2 is not -CH_2CH_2NH when R1, R4 and R5 are CH_3 and R3 and R6 are H; R2 is not



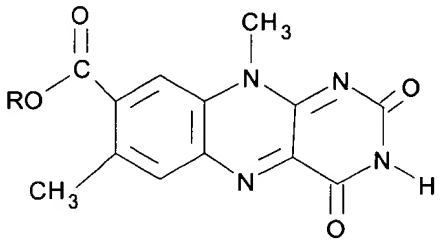
when R1, R4 and R5 are CH_3 and R3 and R6 are H; R5 is not chloro when R4 is methoxy and R1 is ethyl-2'N-pyrrolidino and R2, R3, and R6 are hydrogen; R1 is not N,N-dimethylaminopropyl or N,N-diethylaminoethyl when R5 is chloro or methyl and R2, R3, R4 and R6 are hydrogen; R3 is not -$NH(CH_2CH_2)Cl$ when R6 is -NH2 and R1, R2, R4 and R5 are H; R1, R4, R5 are not all methyl groups when all of R2, R3 and R6 are hydrogens; R1 and R2 are not both methyl groups when R3, R4, R5 and R6 are H; R1, R4, R5 and R2 are not all methyl groups when R3 and R6 are hydrogens; R2 [is not carboxymethyl] does not contain a carbonyl group when R1, R4 and R5 are methyl and R3 and R6 are hydrogen; R4 is not -NH2 when R1 and R5 are methyl and R2, R3 and R6 are all hydrogen; R1 is not a phenyl group when R4 and R5 are methyl and R2, R3 and R6 are all H; R1 is not methyl or N,N-dimethylaminoethyl when all of R2, R3, R4, R5 and R6 are hydrogen; R2, R4, R5 are not all methyl when R1 is acetoxyethyl and R3 and R6 are hydrogen; R5 is not methyl when R1 is N,N-diethylaminoethyl and R2, R3, R4 and R6 are all hydrogen; R4 and R5 are not both chlorine when R1 is methyl and R2, R3 and R6 are all hydrogen; R1 is not ethyl, β-chloroethyl, n-butyl, anilino, benzyl, phenyl, p-tolyl or p-anisyl when R5 is NH_2 and R2, R3, R4 and R6 are all hydrogen; and R4 is not chlorine when R1 is N,N-dimethylaminopropyl and R2, R3, R5 and R6 are

all hydrogen;

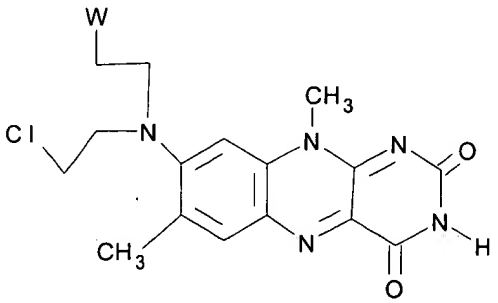
provided that the compound is not:



wherein R is selected from the group consisting of hydrogen and optionally substituted straight chain or branched alkyl having from 1 to 20 carbon atoms; and provided that the compound is not:



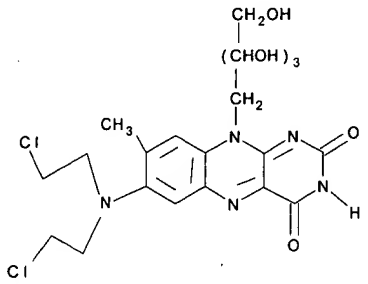
wherein R is selected from the group consisting of hydrogen and optionally substituted straight chain or branched alkyl having from 1 to 20 carbon atoms; and provided that the compound is not:



wherein W is a water soluble group; and provided that R4 is not -OH, -Br, -Cl, -SH, -O-Alk, or -

SAlk when R5 is CH3; R6, R3 and R2 are H and when R1 is Alk or H, where Alk is an alkyl chain of 1 to 4 carbon atoms; provided that R2 is not a 11 carbon straight chain alkyl group when R1, R3, R6 are H and R4 and R5 are methyl; and provided that R2 is not octadecyl or undecyl when R4 and R5 are methyl and [R1,] R3 and R6 are hydrogen; and provided that R2 is not a benzyl group when R1, R4 and R5 are methyl; and R3 and R6 are hydrogen; and provided that R1 or R2 do not contain a poly(pyrrolecarboxaminde) group; and provided that R5 is not bromo, chloro, nitro or trifluoromethyl when R2 is hydrogen, methyl, hydroxyethyl or benzyl and R3 and R6 are hydrogen and R1 is ethyl, propyl, isopropyl, butyl, pentyl, hexyl, phenyl, benzyl, phenehtyl, naphthyl, p-tolyl, p-ethylphenyl, p-anisyl, p-ethoxyphenyl, p-butoxyphenyl, 3,4-dicholorophenyl, methoxyethyl or ethoxyethyl; and provided that R1 is not a five carbon alkyl chain where four carbons are substituted with -O-COR where RCO is a straight chain alkanoyl group containing from 4 to 20 carbon atoms; and provided that R1 is not a phosphoric acid substituted hydroxyalkyl group when R2, R3, R4, R5 and R6 are hydrogen; and provided that R1 is not a two to six member alkyl chain terminated with a sulfate radical, a phosphate radical or an acyloxy radical, the acyl group of which is derived from an organic acid with not more than eighteen carbon atoms.

62. (once amended) The compound [of claim 39] having the structure:



63. (once amended) The compound [of claim 39] having the structure: